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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/393,066	02/23/1995	JOHN H. WOLFE	PENN-0065	1030

7590 01/28/2004

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/393,066	WOLFE ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 February 1995* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The request filed on October 31, 2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/393,066 is acceptable and a CPA has been established. An action on the CPA follows.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons present in the office action mailed May 2, 2003.

Claims 1-9 are drawn to a method of stably expressing a selected DNA sequence in the central nervous system of a mammal, comprising administering to peripheral neuron cells of a mammal a neurotropic virus which infects cells of central nervous system of the mammal, the vector containing a selected DNA sequence operatively linked to a selected promoter so that the selected DNA sequence is stably expressed by infected central nervous system cells for at least four months by the infected central nervous system cells, to a method of stably expressing β-glucuronidase in the brain of a mammal comprising administering to the mammal a neurotropic viral vector which infects cells of the brain of the mammal, said vector being and HSV-1 vector containing a DNA sequence encoding β-glucuronidase operatively linked to a LAT promoter, so that the infected brain cells stably express β-glucuronidase.

While the claimed invention requires only stable expression of the selected DNA sequence, the specification provides no use for mere stable expression. The specification is very clear that the purpose of the delivery method to produce a gene therapy (specification,

page 2, line 3 to page 3, line 17; page 8, lines 9-13; page 9, line 34 to page 10, line 9; page 16, lines 1-17 and page 20, lines 7-10). Thus, the rejection of the claims as not enabled for gene therapy is clearly appropriate. Applicant is asked to point to page and line number where an alternate use is disclosed.

With regards to this rejection, in the response of August 4, 2003, applicant argues that MPEP 2164.01 states that enablement is whether one of skill in the art could make or use the invention when the disclosure is coupled with teachings in the art. Applicant continues in arguing that gene therapy is not the only use for claimed method of delivery; an animal model could also be produced using the claimed method. Applicant argues that any enabled use is sufficient to preclude an enablement rejection. These arguments are not persuasive.

The examiner maintains that the only use disclosed for the claimed method of delivery is for gene therapy. In this regard, the examiner stands behind the enablement rejection of record. This is discussed in detailed below in response to additional applicant arguments.

Applicant's reading of MPEP 2164.01 is incorrect. This section of the MPEP stating that only one enabled use for a product is required, but the present claims are to a method. (See MPEP 2164.01(c). There is no MPEP guidance as to how many uses need to be enabled for a method.

> "when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention."

Further, applicant's filing of evidence that at the time of filing, it would have been readily apparent to the skilled artisan that the claimed method could be used to produce an animal model of a disease is not persuasive. Applicant is to fully comprehend the uses of their invention at the time the application is filed. The art supplied, Xing et al. is post-filing. While the examiner appreciates that applicant was trying to overcome a rejection using Xing as evidence, the situation remains that the specification makes no mention of using the claimed method to produce an animal model. The specification does not suggest nor provide guidance as to what the animal is to model, what genes or DNA sequence could be used to produce such a model, or what species animal is to be used. A post-filing publication cannot be used to establish a readily apparent use at the time of filing. Further, Xing discloses the production of a mouse model to study IL-6 biologic functions at local tissue sites by the intra-tracheal instillation of an adenovirus comprising a DNA sequence for IL-6. This model is clearly not related to any animal model produced by the claimed method. Applicant has not established any other well-known uses for the claimed method at the time of filing. This burden lies with applicant. The examiner is to review the record, and not to supply teachings omitted from the specification as filed.

Applicant argues that the use of Verma, Marshall, Anderson and Blau to support the lack of enablement rejection does not fully address the state of neurotropic viruses. Applicant argues that Wolfe, while stating that too little β-glucuronidase was expressed to measure enzymatic activity, they state that the intensity of staining correlates with quantitative measurements of enzymatic activity and that the cells may have been expressing nearly normal amounts of GUSB. Applicant further argues that in US Patent 5,849,572 that lacZ expression from and HSV-LAT-LacZ vector was present 6 months post-inoculation and that LacZ stating increases over time. These arguments are not persuasive.

The cite art of Fink et al, Wolf et al and '572 are each drawn to HSV-LAT vectors. Applicant's claims are broader that this. However, there is no evidence that the level of expression was therapeutic.

Further, the specification does not provide guidance for other vectors and promoters for use in methods of treatment where a prediction of success can be made. The method states that the vector is administer to a peripheral neuron. The means through which a virus can infect the CNS, as required by the claim, by peripheral neuron infection is by retrograde transport. Of the vectors specifically disclosed only HSV and rabies are recognized by the art as being transported to the CNS by retrograde transport. The specification teaches that the LAT promoter gives measure gene expression for fourth months, but does not provide guidance for any other promoter to express for this length of time. The LAT promoter is specific for HSV, and is not found in rabies, or any other virus. The LAT promoter is active only during the latent phase of HSV infection, and this phase is not described for other viruses. The specific mechanism for activation of the LAT promoter is not known for rabies virus, and thus the use of rabies virus with the claimed invention is unpredictable.

The claims are free of the prior art. At the time of filing the cited prior art did not teach or suggest the administration of a viral vector to a peripheral neuron cell with a neurotropic vector comprising a DNA sequence operably linked to a promoter would result in stable expression for at least four months.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Reynolds, SPE of AU 1632 whose telephone number 703-305-4051. The examiner can normally be reached on M-Th.

Should inquiries be made on or after January 12, 2004, the examiner's phone number will be 571-272-0727. Deborah Reynolds will be reached at 571-272-0734.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 for regular and After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

January 23, 2004